

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau



(43) International Publication Date  
15 July 2004 (15.07.2004)

PCT

(10) International Publication Number  
**WO 2004/058305 A3**

(51) International Patent Classification<sup>7</sup>: C12N 11/04, A61K 35/00 (74) Agent: RIDOUT & MAYBEE LLP; One Queen Street East, Suite 2400, Toronto, Ontario M5C 3B1 (CA).

(21) International Application Number: PCT/CA2003/002008 (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(22) International Filing Date: 24 December 2003 (24.12.2003) (84) Designated States (*regional*): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

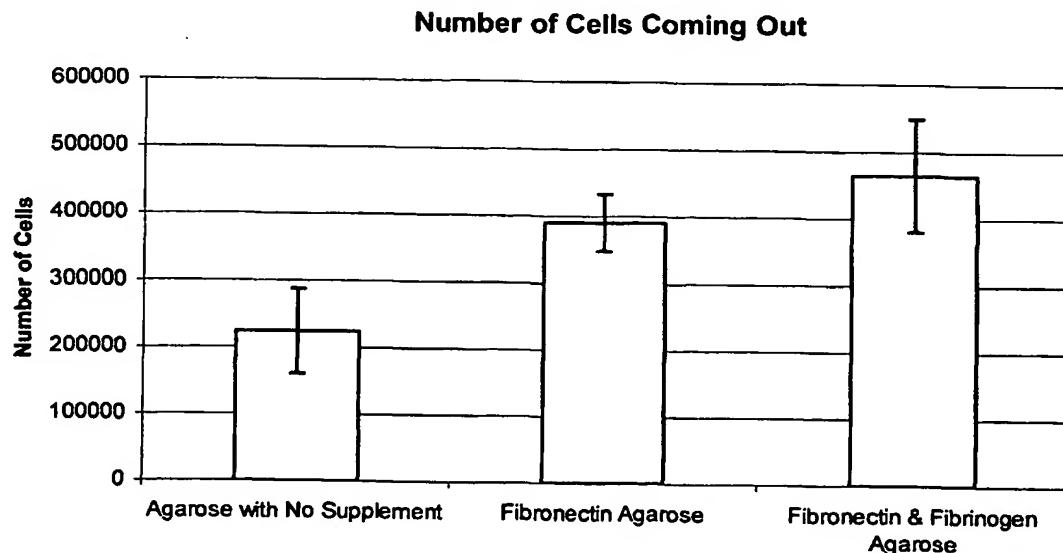
(25) Filing Language: English (26) Publication Language: English (Published: — with international search report)

(30) Priority Data: 60/435,858 24 December 2002 (24.12.2002) US (88) Date of publication of the international search report: 31 March 2005

(71) Applicant (*for all designated States except US*): AN-GO-GEN INC. [CA/CA]; 438 University Avenue, Suite 300, Toronto, Ontario M5G 2P9 (CA). For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(71) Applicants and (72) Inventors: STEWART, Duncan, J. [CA/CA]; St. Michael's Hospital, 30 Bond Street, 7-081 - Queen Wing, Toronto, Ontario M5B 1W8 (CA). COURTMAN, David [CA/CA]; 30 Bond Street, 7-081 - Queen Wing, Toronto, Ontario M5B 1W8 (CA). KAROUBI, Golnaz [CA/CA]; 361 Willowdale Avenue, Toronto, Ontario M2N 5A5 (CA).

(54) Title: ENCAPSULATED CELL FOR THERAPY



(57) Abstract: Cell therapy comprises encapsulating a cell with an integrin or other cell interaction factor, for administration to a mammal. The cells may express a therapeutic transgene or the cells may be regenerative.

WO 2004/058305 A3

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/CA 03/02008

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 C12N11/04 A61K35/00

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, MEDLINE, BIOSIS

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>RAMDI HAFIDA ET AL: "Influence of matricial molecules on growth and differentiation of entrapped chondrocytes" EXPERIMENTAL CELL RESEARCH, vol. 207, no. 2, 1993, pages 449-454, XP002275507 ISSN: 0014-4827 page 449, left-hand column, paragraph 1 - right-hand column, paragraph 1 page 450, left-hand column, paragraphs 1,2 page 451, right-hand column, paragraph 2 page 452, left-hand column, paragraph 2 page 453, right-hand column - page 454, paragraph 4</p> <p>-----</p> <p>-/-</p>	1,2, 10-37

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the International filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the International filing date but later than the priority date claimed

- "T" later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

30 March 2004

Date of mailing of the international search report

07.09.2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Sitch, W

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/CA 03/02008

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE BIOSIS [Online]          BIOSCIENCES INFORMATION SERVICE,          PHILADELPHIA, PA, US; 1995,          JAIN KANTI ET AL: "Retrievable,          replaceable, macroencapsulated pancreatic          islet xenografts"          XP002275511          Database accession no. PREV199598235605          abstract          &amp; TRANSPLANTATION (BALTIMORE),          vol. 59, no. 3, 1995, pages 319-324,          ISSN: 0041-1337</p> <p>-----</p>	1,2, 10-37
X	<p>WO 98/05304 A (LI REBECCA          ;CYTOTHERAPEUTICS INC (US); HAZLETT TYRONE          F (US)) 12 February 1998 (1998-02-12)          page 3, line 17 - page 4, line 29          page 8, line 9 - page 9, line 23</p> <p>-----</p>	1,2, 10-37
X	<p>WO 95/19430 A (JAIN KANTI ;ROGOSIN INST          (US); RUBIN ALBERT L (US))          20 July 1995 (1995-07-20)          page 5, line 1 - line 27          page 10, line 26 - page 11, line 19          page 15, line 15 - line 24</p> <p>-----</p>	1,2, 10-37
A	<p>DATABASE MEDLINE [Online]          US NATIONAL LIBRARY OF MEDICINE (NLM),          BETHESDA, MD, US;          MARLER ET AL: "Soft-tissue augmentation          with injectable alginate and syngeneic          fibroblasts"          XP002275512          Database accession no. NLM10839402          abstract          &amp; PLASTIC AND RECONSTRUCTIVE SURGERY,          vol. 105, 2000, pages 2049-2058,</p> <p>-----</p>	
A	<p>DATABASE MEDLINE [Online]          US NATIONAL LIBRARY OF MEDICINE (NLM),          BETHESDA, MD, US;          HALBERSTADT ET AL: "A hydrogel material          for plastic and reconstructive          applications injected into the          subcutaneous space of a sheep"          XP002275513          Database accession no. NLM12031119          abstract          &amp; TISSUE ENGINEERING,          vol. 8, April 2002 (2002-04), pages          309-319,</p> <p>-----</p> <p style="text-align: center;">-/-</p>	

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/CA 03/02008

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>DATABASE BIOSIS [Online]          BIOSCIENCES INFORMATION SERVICE,          PHILADELPHIA, PA, US; July 2002 (2002-07),          PARK KEUN-HONG: "Improved long-term          culture of hepatocytes in a hydrogel          containing Arg-Gly-Asp (RGD)"          XP002275514</p> <p>Database accession no. PREV200200500968          abstract</p> <p>&amp; BIOTECHNOLOGY LETTERS,          vol. 24, no. 14, July 2002 (2002-07),          pages 1131-1135,          ISSN: 0141-5492</p> <p>-----</p>	
A	<p>BURDICK JASON A ET AL:          "Photoencapsulation of osteoblasts in          injectable RGD-modified PEG hydrogels for          bone tissue engineering"          BIOMATERIALS,          vol. 23, no. 22, November 2002 (2002-11),          pages 4315-4323, XP002275508          ISSN: 0142-9612</p> <p>page 4316, left-hand column, paragraph 5 -          right-hand column, paragraph 1</p> <p>page 4321, right-hand column, paragraphs          1,2</p> <p>page 4322, left-hand column, paragraph 2</p> <p>-----</p>	
A	<p>NUTTELMAN CHARLES R ET AL: "Attachment of          fibronectin to poly(vinyl alcohol)          hydrogels promotes NIH3T3 cell adhesion,          proliferation, and migration"          JOURNAL OF BIOMEDICAL MATERIALS RESEARCH,          vol. 57, no. 2, November 2001 (2001-11),          pages 217-223, XP002275509          ISSN: 0021-9304</p> <p>page 217          abstract</p> <p>-----</p>	
A	<p>MANN BRENDA K ET AL: "Smooth muscle cell          growth in photopolymerized hydrogels with          cell adhesive and proteolytically          degradable domains: Synthetic ECM analogs          for tissue engineering"          BIOMATERIALS,          vol. 22, no. 22, November 2001 (2001-11),          pages 3045-3051, XP002275510          ISSN: 0142-9612</p> <p>page 3045          abstract</p> <p>page 3047, right-hand column, paragraph 2</p> <p>-----</p>	-/-

## INTERNATIONAL SEARCH REPORT

International Application No PCT/CA 03/02008
---

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>DATABASE BIOSIS [Online]          BIOSCIENCES INFORMATION SERVICE,          PHILADELPHIA, PA, US;          January 1999 (1999-01),          ROWLEY JON A ET AL: "Alginate hydrogels as          synthetic extracellular matrix materials"          XP002275515          Database accession no. PREV199900058021          abstract          &amp; BIOMATERIALS,          vol. 20, no. 1, January 1999 (1999-01),          pages 45-53,          ISSN: 0142-9612</p> <p>-----</p>	
P,A	<p>DATABASE MEDLINE [Online]          US NATIONAL LIBRARY OF MEDICINE (NLM),          BETHESDA, MD, US;          KOH ET AL: "Molding of hydrogel          microstructures to create multiphenotype          cell microarrays"          XP002275516          Database accession no. NLM14588018          abstract          &amp; ANALYTICAL CHEMISTRY,          vol. 75, 1 November 2003 (2003-11-01),          pages 5783-5789,</p> <p>-----</p>	
P,A	<p>KAROUBI GOLNAZ ET AL: "Cell          micro-encapsulation with integrin binding          proteins prevents anoikis: Implications          for adherent cell therapy."          CIRCULATION,          vol. 108, no. 17 Supplement,          28 October 2003 (2003-10-28), pages          IV-286, XP008029277          American Heart Association Scientific          Sessions 2003;Orlando, FL, USA; November          09-12, 2003          ISSN: 0009-7322 (ISSN print)          abstract</p> <p>-----</p>	

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/CA 03/02008

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:  
**Although claims 24, 25, 28, 29 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.**
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Partially 1, 2, 10-37

### Remark on Protest

The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 24, 25, 28, 29 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: Partially 1, 2, 10-37

A method of encapsulating a cell, wherein the method used results in the encapsulation product including an 'integrin binding partner', and wherein said 'integrin binding partner' is a collagen; use of products obtainable thereby, kit for use therein

---

2. claims: Partially 1, 2, 10-37; completely 3-5, 9

As 1, but wherein the 'integrin binding partner' is selected from the group consisting of fibronectin, vitronectin, von Willebrand Factor, tenascin, laminin, fibrinogen, thrombospondin, an RGD [1 letter amino acid code used] containing peptide, fibrin, and insofar as the subject matter of the invention does not relate to any in any of the other inventions listed herein

---

3. claims: Partially 1, 2, 10-37

As 1, but wherein the 'integrin binding partner' is a peptide containing the sequence LDV [1 letter amino acid code used], and insofar as the subject matter of the invention does not relate to any in any of the other inventions listed herein

---

4. claims: Partially 1, 2, 10-37

As 1, but wherein the 'integrin binding partner' is a peptide containing the sequence HHLGGAKQAGDV [1 letter amino acid code used], and insofar as the subject matter of the invention does not relate to any in any of the other inventions listed herein

---

5. claims: Partially 1, 2, 10-37

As 1, but wherein the 'integrin binding partner' is selected from the group consisting of VCAM-1, MAdCAM-1, LFA-1, Mac-1, ICAM-1, ICAM-2, ICAM-3, complement component C3bi, and insofar as the subject matter of the invention does not relate to any in any of the other inventions listed herein

---

6. claims: Partially 1, 2, 10-37; completely 6-8

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

As 1, but wherein the 'integrin binding partner' is selected from the group consisting of Factor X, FXIII, FXIIIa, and insofar as the subject matter of the invention does not relate to any in any of the other inventions listed herein

---

# INTERNATIONAL SEARCH REPORT

Information on patent family members			International Application No PCT/CA 03/02008	
Patent document cited in search report	Publication date		Patent family member(s)	Publication date
WO 9805304	A	12-02-1998	US 6054142 A AT 250435 T AU 723826 B2 AU 3823697 A CA 2258483 A1 DE 69725149 D1 DE 69725149 T2 DK 918509 T3 EP 0918509 A1 ES 2208938 T3 JP 2000515551 T WO 9805304 A1 US 6231879 B1	25-04-2000 15-10-2003 07-09-2000 25-02-1998 12-02-1998 30-10-2003 03-06-2004 26-01-2004 02-06-1999 16-06-2004 21-11-2000 12-02-1998 15-05-2001
WO 9519430	A	20-07-1995	AU 681240 B2 AU 1526795 A CA 2181156 A1 CN 1141650 A ,B EP 1418228 A1 EP 0742818 A1 FI 962841 A IL 112330 A JP 9510868 T NO 962955 A NZ 278809 A NZ 329619 A RU 2177503 C2 RU 2208636 C2 WO 9519430 A1 US RE38027 E1 US 5643569 A	21-08-1997 01-08-1995 20-07-1995 29-01-1997 12-05-2004 20-11-1996 12-09-1996 26-01-1999 04-11-1997 11-09-1996 25-03-1998 29-09-1999 27-12-2001 20-07-2003 20-07-1995 11-03-2003 01-07-1997